Purpose/Objective(s): Our hypothesis was that pre-treatment inflammation in the lung makes pulmonary tissue more susceptible to radiation damage. The relationship between pre-treatment 18F-fluorodeoxyglucose (FDG) uptake in the lungs (as a surrogate for inflammation), the delivered radiation dose and radiation-induced lung toxicity (RILT) were investigated.

Materials/Methods: We retrospectively studied a prospectively obtained cohort of 101 non-small cell lung cancer (NSCLC) patients treated with (chemo-) radiation therapy (RT). For all patients FDG-PET-CT scans were used for treatment planning. FDG uptake patterns in the lungs, excluding clinical target volume(s) (CTV), were characterized by the following standardized uptake value (SUV) parameters: the mean, maximum, standard deviation and the 80th (SUV80), 90th (SUV90) and 95th (SUV95) percentiles. The fractions of the 5% highest SUV voxels (i.e. all voxels with SUV > SUV95) that were within the lung volumes receiving more than 2, 5, 10 or 20 Gy (V2, V5, V10, V20) were calculated (F2, F5, F10, F20) to investigate the effect of dose to high SUV regions. An increase in dyspnea grade (CTCAEv3.0) of 1 or more points compared to the pre-RT score was used as endpoint of RILT. The relation between FDG uptake, lung density measured with CT, other patient characteristics and RILT was studied with logistic regression. Because the absolute SUV values can vary considerably among patients, the effect of dose to the 5% highest SUV voxels was determined by testing the interaction terms SUV95 times F2, SUV95 times F5, SUV95 times F10 and SUV95 times F20.

Results: An increased density and FDG uptake in the lungs, excluding CTV, before RT were related to an increased risk of RILT after RT with univariable logistic regression (p < 0.05). The 95th percentile of the FDG uptake remained significant with multivariable logistic regression (p = 0.016, Odds ratio (OR) = 4.3), together with age (p = 0.029; OR = 1.06) and dyspnea pre-RT score >=1 (p = 0.005; OR = 0.20). Significant interaction effects were demonstrated between the SUV95 and the fractions of the 5% highest SUV voxels that received more than 2 Gy (p = 0.015) and 5 Gy (p = 0.046). For example, if the fraction that received more than 5 Gy was 50% the OR of SUV95 was 2.8, compared to an OR of 91 for a fraction of 90%.

Conclusions: The risk of RILT increased with increasing FDG uptake in the lungs excluding CTV. The effect became more pronounced as the fraction of the 5% highest SUV voxels that received more than 2 - 5 Gy increased. Our findings may enable both the selection of patients at high risk for RILT and strategies to decrease the risk by using radiotherapy techniques that can avoid areas in the lung with high FDG uptake.

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